

**CLAIMS**

1. A hyperbranched amidoamine polymer comprising [A] a first structural repeating unit having a connectivity of three consisting of a nitrogen core linked to a first amidoamine unit, a second amidoamine unit and a third amidoamine unit, [B] a second structural repeating unit having a connectivity of two consisting of a nitrogen core linked to a first amidoamine unit and a second amidoamine unit and [C] terminal units of which a major portion comprises amine groups or a functional derivative thereof, and a minor portion comprises carboxylic acid or related groups or a functional derivative thereof.
- 15 2. A polymer according to claim 1, wherein the ratio of structural repeating units having a connectivity of three to structural repeating units having a connectivity of two and terminal units is in the range of 1:10:20 to 1:2:2.5.
- 20 3. A hyperbranched amidoamine polymer whose molecules are characterised by a nitrogen core linked to:
  - a first irregularly branched amidoamine unit terminating in an amine group or a functional derivative thereof:
  - a second irregularly branched amidoamine unit terminating in a amine group or a functional derivative thereof: and
  - a third irregularly branched amidoamine unit terminating in a carboxylic acid or related group or a functional derivative thereof.
- 25
- 30

4. A polymer according to claim 1, selected from the group consisting of hyperbranched amidoamine polymers having a theoretical degree of branching of up to 50%, hyperbranched amidoamine polymers having a theoretical degree of branching of up to 67%, hyperbranched amidoamine polymers having a theoretical degree of branching of up to 75% and hyperbranched amidoamine polymers having a theoretical degree of branching of up to 80%.

10

5. A polymer according to claim 3, selected from the group consisting of hyperbranched amidoamine polymers wherein each of the first, second and third irregularly branched amidoamine units includes consecutive, 15 irregularly branched aminoamine moieties each having two or more amido groups and hyperbranched amidoamine polymers wherein the amine group or functional derivative thereof in which the first and second irregularly branched amidoamine unit terminates is a primary amine 20 group or a functional derivative thereof.

6. A polymer according to claim 5, selected from the group consisting of hyperbranched amidoamine polymers wherein the functional derivative is selected from the 25 group consisting of secondary, tertiary, and quaternary amine groups, aromatic and aliphatic amide groups, cyano groups, sulphur containing groups, cross-linking groups, anilino groups and acyclic polynitrogen groups, and hyperbranched amidoamine polymers wherein the functional 30 derivative is an amine group selected from the group consisting of amine groups substituted with one, two and three C<sub>1-6</sub> - alkyl groups, and amine groups substituted with an N, N - substituted amidoamine group.

7. A polymer according to claim 6, in which the functional derivative is a quaternary amine group.

5 8. A polymer according to claim 1, wherein the related group of the carboxylic acid is selected from the group consisting of a salt, ester, anhydride, acid halide, acyl, amide, imide, nitrile, aldehyde and a hydrazide group.

10 9. A polymer according to claim 1, wherein the functional derivative of the carboxylic acid is selected from the group consisting of carboxyl protecting and blocking groups and groups chosen to suit the desired function of 15 the polymer.

10. A polymer according to claim 3, wherein the third irregularly branched amidoamine unit terminates in a terminal group selected from the group consisting of 20 carboxylic acid groups and functional derivatives thereof.

11. A hyperbranched amidoamine polymer of formula I:

(I) 
$$\begin{array}{c} \text{R}^1\text{T}^1 \\ \diagdown \\ \text{T}-\text{R}^3-\text{CO}-\text{Y}-\text{N} \\ \diagup \\ \text{R}^2 \end{array}$$

25 wherein:

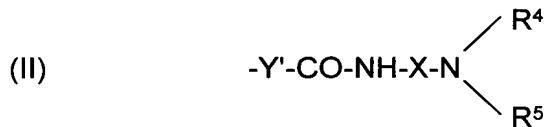
Y is a divalent bridging group;

T together with a terminal CO group of R<sup>3</sup> to which it is bound is a carboxylic acid or related group or a 30 functional derivative thereof;

$T^1$  together with a terminal nitrogen atom of  $R^1$  to which it is bound is an amine group or a functional derivative thereof;

$R^1$  is an amidoamine unit of formula II;

5



wherein:

each of  $X$  and  $Y'$  which may be the same or different  
10 is a divalent bridging group;

$R^4$  is selected from the group consisting of

(a)  $n$  consecutive amidoamine moieties of formula  
III;

15



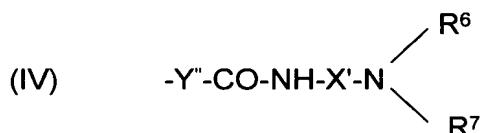
wherein:

$s$  is 0 or 1;

$n$  is a number greater than 0;

20 each of  $X'$  and  $Y''$  which may be the same or different is a  
divalent bridging group, and  
(b) an amidoamine unit of formula IV;

25



wherein:

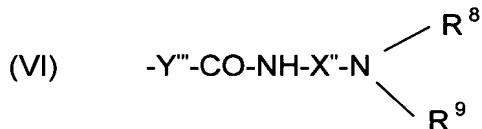
$R^6$  is selected from the group consisting of

(a)  $m$  consecutive amidoamine moieties of formula V:

(V)  $-Y'''-CO-NH-X''-NH-CO-Y-NR^2-Y'-CO-NH-X-NR^5-Y''-CO-NH-X'-NR^7-$

wherein:

5 m is a number greater than 0;  
 each of X'' and Y''' which may be the same or different is a  
 divalent bridging group and  
 (b) an amidoamine unit of formula VI:



10

wherein:

R<sup>8</sup> is x consecutive amidoamine moieties of formula VII:

-Y''''-CO-NH-X'''-NH-CO-Y-NR<sup>2</sup>-Y'-CO-NH-X-NR<sup>5</sup>-Y''-CO-NH-X'-  
 15 NR<sup>7</sup>-Y'''-CO-NH-X''-NR<sup>9</sup>  
 (VII)

wherein:

X is a number greater than 0;  
 Each of X''' and Y'''' which may be the same or different is  
 20 a divalent bridging group; and

R<sup>9</sup> is selected from the group consisting of R<sup>1</sup> T<sup>1</sup>, a group  
 as hereinbefore defined for R<sup>8</sup>T<sup>1</sup> wherein T<sup>1</sup> together with a  
 terminal nitrogen atom of R<sup>8</sup> to which it is bound is an  
 amine group, and a group as hereinbefore defined for R<sup>8</sup>T<sup>1</sup>  
 25 wherein T<sup>1</sup> together with a terminal nitrogen atom of R<sup>8</sup> to  
 which it is bound is a functional derivative of an amine  
 group;

R<sup>7</sup> is selected from the group consisting of R<sup>1</sup> T<sup>1</sup>, a group  
 as hereinbefore defined for R<sup>6</sup>T<sup>1</sup> wherein T<sup>1</sup> together with a  
 30 terminal nitrogen atom of R<sup>6</sup> to which it is bound is an  
 amine group, and a group as hereinbefore defined for R<sup>6</sup>T<sup>1</sup>

wherein  $T^1$  together with a terminal nitrogen atom of  $R^6$  to which it is bound is a functional derivative of an amine group;

$R^5$  is selected from the group consisting of  $R^1 T^1$ , a group as hereinbefore defined for  $R^4 T^1$  wherein  $T^1$  together with a terminal nitrogen atom of  $R^4$  to which it is bound is an amine group, and a group as hereinbefore defined for  $R^4 T^1$  wherein  $T^1$  together with a terminal nitrogen atom of  $R^4$  to which it is bound is a functional derivative of an amine group;

$R^2$  is as hereinbefore defined for  $R^1 T^1$ ; and  
 $R^3$  is selected from the group consisting of

(a)  $p$  consecutive amidoamine moieties of formula VIII:

(VIII) 
$$-\text{CO}-Y-\text{NR}^2-\text{Y}'-\text{CO}-\text{NH}-X-\text{NR}^5-\text{Y}''-\text{CO}-\text{NH}-X'-\text{NR}^7-\text{Y}'''-\text{CO}-\text{NH}-X''-\text{NH}-$$

wherein:

$p$  is a number of more than zero;

(b)  $q$  consecutive amidoamine moieties of formula IX:

(IX) 
$$-\text{CO}-Y-\text{NR}^2-\text{Y}'-\text{CO}-\text{NH}-X-\text{NR}^5-\text{Y}''-\text{CO}-\text{NH}-X'-\text{NR}^7-\text{Y}'''-\text{CO}-\text{NH}-X''-\text{NH}-$$

wherein:

25  $q$  is a number greater than 0, and

(c)  $y$  consecutive amidoamine moieties of formula X:

$$-\text{CO}-Y-\text{NR}^2-\text{Y}'-\text{CO}-\text{NH}-X-\text{NR}^5-\text{Y}''-\text{CO}-\text{NH}-X'-\text{NR}^7-\text{Y}'''-\text{CO}-\text{NH}-X''-\text{NRO}-\text{Y}''''-\text{CO}-\text{NH}-X''''-\text{NH}-$$

30 (X)

wherein:

$y$  is a number greater than 0.

12. A polymer according to claim 11, selected from the group consisting of hyperbranched amidoamine polymers wherein R<sup>1</sup> T<sup>1</sup> is the same as R<sup>2</sup>, hyperbranched amidoamine polymers wherein R<sup>4</sup> T<sup>1</sup> is the same as R<sup>5</sup>, hyperbranched amidoamine polymers wherein R<sup>6</sup> is the same as R<sup>7</sup>, and hyperbranched amidoamine polymers wherein R<sup>8</sup> is the same as R<sup>9</sup>.

10 13. A polymer according to claim 12, selected from the group consisting of hyperbranched amidoamine polymers wherein R<sub>4</sub> is option (a) and s is 0, hyperbranched amidoamine polymers wherein R<sub>4</sub> is option (a) and s is 1, hyperbranched amidoamine polymers wherein R<sub>4</sub> is option 15 (b) and R<sub>6</sub> is option (a), hyperbranched amidoamine polymers wherein R<sub>4</sub> is option (b) and R<sub>6</sub> is option (b), and hyperbranched amidoamine polymers wherein n + p or m + q or x + y is in the range of from 1 to 20.

20 14. A polymer according to claim 11, wherein each of Y, Y', Y'', Y''', Y'''', X, X', X'' and X''', which may be the same or different, is selected from the group consisting of a cyclic hydrocarbon bridging group, an acyclic heteroatomic bridging group, a heterocyclic bridging 25 group, and an acyclic hydrocarbon bridging group, which itself may be optionally interrupted by or may terminate in one or more groups selected from the group consisting of a cyclic hydrocarbon group, an acyclic heteroatomic group, a heterocyclic group, and an amide group.

30 15. A polymer according to claim 11, wherein each of Y, Y', Y'', Y''', Y'''', X, X', X'' and X''', which may be the same or different, is selected from the group consisting

of  $C_{1-12}$  - alkylene and  $C_{1-12}$  - alkenylene bridging groups wherein said bridging groups are optionally interrupted by or terminating in an atom or group selected from the group consisting of oxygen atoms, one, two and three 5 optionally substituted nitrogen atoms, cyclic hydrocarbon groups, heterocyclic groups, and amide groups.

16. A polymer according to claim 15, wherein each of  $Y$ ,  $Y'$ ,  $Y''$ ,  $Y'''$ ,  $Y''''$ ,  $X$ ,  $X'$ ,  $X''$  and  $X''''$ , which may be the 10 same or different, is selected from the group consisting of  $C_{1-6}$  - alkylene bridging groups,  $C_{1-4}$  - alkylene bridging groups and ethylene.

17. A polymer according to claim 11, wherein  $T$  is 15 selected from the group consisting of  $Cl$ ,  $O-CO-R^{10}$ ,  $NHR^{12}$ ,  $=NH$ ,  $\equiv N$ ,  $H$ ,  $OR^{11}$  and  $OMet$ , wherein each of  $R^{10}$  and  $R^{11}$ , which may be the same or different, is selected from the group consisting of hydrogen and an optionally substituted  $C_{1-12}$ -alkyl group;  $R^{12}$  is selected from the 20 group consisting of hydrogen, an optionally substituted  $C_{1-12}$ -alkyl group and  $NHR^{10}$ , and  $Met$  is a metal.

18. A polyamidoamine according to claim 17, wherein  $T$  is 25 a hydroxyl group.

19. A polyamidoamine according to claim 11, wherein  $T^1$  is selected from the group consisting of hydrogen and  $N$  - substituents rendering the nitrogen to which they are bound a functional derivative of an amine group.

30 20. A process for preparing a hyperbranched amidoamine polymer comprising:

(A) inducing polymeric condensation of a compound in which a nitrogen core is linked to:

5 a first amidoamine unit selected from the group consisting of amidoamine, (N - amidoamine) amidoamine, N - (N - amidoamine) amidoamine, and N-(N - (N - amidoamine) amidoamine) amidoamine units terminating in an amine group;

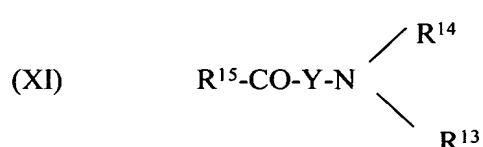
10 a second amidoamine unit selected from the group consisting of amidoamine, (N - amidoamine) amidoamine, N - (N - amidoamine) amidoamine, and N-(N - (N - amidoamine) amidoamine) amidoamine units terminating in an amine group; and

15 a third unit terminating in a group selected from the group consisting of carboxylic acid and related groups.

21. A process according to claim 20, wherein the terminal amine group is a primary amine group.

20 22. A process according to claim 22, wherein the third unit is selected from the group consisting of carboxylic acid groups and carboxylic acid salt, ester, anhydride, acide halide, acyl, amide, imide, nitrile, aldehyde and hydrazide groups.

25 23. A process according to claim 20, which comprises inducing polymeric condensation of a compound of formula:



wherein:

Y is as hereinbefore defined;

$R^{15}$  is as hereinbefore defined for group T;

5 Each of  $R^{13}$  and  $R^{14}$ , which may be the same or different, is selected from the group consisting of  $-Y'-CO-NH-X-NH_2$  and  $-Y'-CO-NH-X-NR^{16}(Y''-CO-NH-X'-NR^{17}R^{18})$  wherein  $R^{16}$  is selected from the group consisting of hydrogen and  $-Y''-CO-NH-X'-NR^{17}R^{18}$ , each of  $R^{17}$  and  $R^{18}$ , which may be the same or different, is selected from the group consisting of hydrogen and  $-Y'''-CO-NH-X''-NR^{19}R^{20}$  wherein each of  $R^{19}$  and  $R^{20}$ , which may be the same or different, is selected from the group consisting of hydrogen and  $-Y''''-CO-NH-X''''-NH_2$ , and

10 15  $Y', X, X', X'', X''', Y''', Y''''$  and  $Y''$  are as hereinbefore defined.

24. A process according to claim 23, wherein  $R^{15}$  is hydroxyl.

20

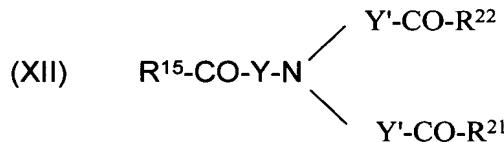
25. A process according to claim 23, wherein the compound is selected from the group consisting of compounds wherein  $R^{13}$  and  $R^{14}$  are both the group  $-Y'-CO-NH-X-NH_2$ , compounds wherein  $R^{13}$  and  $R^{14}$  are both the group  $-Y'-CO-NH-X-N-(Y''-CO-NH-X'-NH_2)_2$ , compounds wherein  $R^{13}$  and  $R^{14}$  are both the group  $-Y'-CO-NH-X-N-(Y''-CO-NH-X'-N(Y''-CO-NH-X''-NH_2)_2)_2$ , and compounds wherein  $R_{13}$  and  $R_{14}$  are both the group  $-Y'-CO-NH-X-N-(Y''-CO-NH-X'-N(Y''-CO-NH-X''-N(Y''-CO-NH-X''-N(Y''-CO-NH-X''-NH_2)_2)_2)_2$ .

30

26. A process according to claim 20, wherein step (A) is preceded by:

(AO) reacting a diamine of formula  $\text{NH}_2\text{-X-NH}_2$  with a compound of formula:

5



wherein:

10  $\text{R}^{21}$  and  $\text{R}^{22}$ , which may be the same or different, are as hereinbefore defined for group T, and  $\text{Y}'$ ,  $\text{R}^{15}$  and Y are as hereinbefore defined.

27. A process according to claim 26, wherein each of  $\text{R}^{21}$   
15 and  $\text{R}^{22}$  is an  $\text{OC}_{1-6}$ -alkyl group.

28. A process according to claim 26, wherein step (AO) is preceded by:

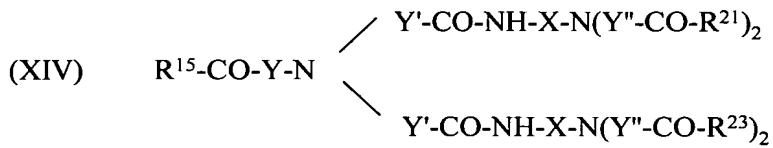
20 (AOO) reacting a compound of formula:



wherein Y and  $\text{R}^{15}$  are as hereinbefore defined, with a  
25 Michael addition reagent.

29. A process according to claim 20, wherein step (A) is preceded by:

(AO') reacting a diamine of formula  $\text{NH}_2\text{-X'-NH}_2$  with a  
30 compound of formula:



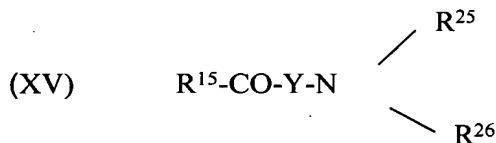
wherein:

5  $R^{23}$  and  $R^{24}$  which may be the same or different, are as hereinbefore defined for group T and X,  $X'$ , Y,  $Y'$  and  $Y''$  are as hereinbefore defined.

30. A process according to claim 29, wherein each of  $R^{23}$   
10 and  $R^{24}$  is an  $OC_{1-6}$  - alkyl group.

31. A process according to claim 29, wherein step (A'0) is preceded by:

(A'OO) reacting a compound of formula:



15

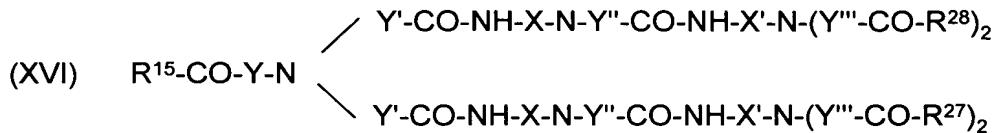
wherein Y and R<sup>15</sup> are as hereinbefore defined; and each of R<sup>25</sup> and R<sup>26</sup>, which may be the same or different, is a group -Y'-CO-NH-X-NH<sub>2</sub> wherein X and Y' are as hereinbefore defined, with a Michael addition reagent.

32. A process according to claim 20, wherein step (A) is preceded by:

25

(A''O) reacting a diamine of formula  $\text{NH}_2-\text{X}''-\text{NH}_2$  with a compound of formula:

5



wherein  $\text{R}^{27}$  and  $\text{R}^{28}$ , which may be the same or different, are as hereinbefore defined for group T, and X, X', X'', Y, Y', Y'' and Y''' are as hereinbefore defined.

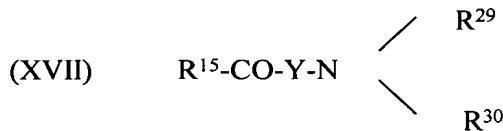
10

33. A process according to claim 32, in which each of  $\text{R}^{27}$  and  $\text{R}^{28}$  is an  $\text{OC}_{1-6}$  alkyl group.

15

34. A process according to claim 32, in which step (A''O) is preceded by:

(A''00) reacting a compound of formula:



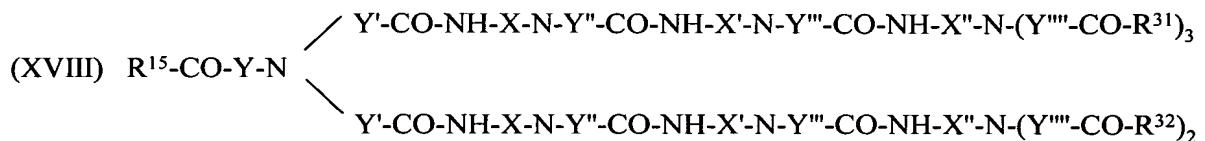
20

wherein Y and  $\text{R}^{15}$  are as hereinbefore defined: and each of  $\text{R}^{29}$  and  $\text{R}^{30}$ , which may be the same or different, is a group  $-\text{Y}'\text{-CO-NH-X-N-Y''-CO-NH-X'-NH}_2$  wherein X, X', Y' and Y'' are as hereinbefore defined, with a Michael addition reagent.

25

35. A process according to claim 20, wherein step (A) is preceded by:

(A'''O) reacting a diamine of formula  $\text{NH}_2-\text{X}'''-\text{NH}_2$  with a compound of formula:

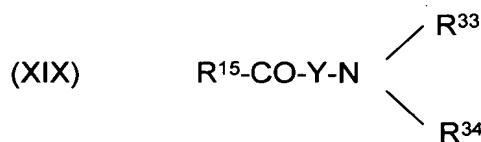


5

wherein  $\text{R}^{31}$  and  $\text{R}^{32}$ , which may be the same or different, are as hereinbefore defined for group T, and X, X', X'', X''', Y, Y', Y'', Y''' and Y'''' are as hereinbefore defined.

10 36. A process according to claim 35, wherein each of  $\text{R}^{31}$  and  $\text{R}^{32}$  is an  $\text{OC}_{1-6}\text{-alkyl}$  group.

15 37. A process according to claim 35, wherein step (A'''O) is preceded by:  
(A'''OO) reacting a compound of formula:



20 wherein Y and  $\text{R}^{15}$  are as hereinbefore defined; and each of  $\text{R}^{33}$  and  $\text{R}^{34}$  is a group-Y'-CO'NH-X-N-Y''-CO-NH-X'-N-Y'''-CO-NH-X''-NH<sub>2</sub> wherein X, X', X'', Y', Y'' and Y''' are as hereinbefore defined, with a Michael addition reagent.

38. A process according to claim 20, in which polymeric condensation is carried out using an amide coupling agent  
5 selected from the group consisting of triphenylphosphite/pyridine, benzotriazol-1-yloxytris(dimethylamino) phosphonium hexafluorophosphate, and 4-(4,6-dimethoxyl-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride.

10

39. A process according to claim 20, which further comprises a step selected from the group consisting of: (B1) functionally derivatising the amine groups in which the first and second irregularly branched amidoamine  
15 units terminate and (B2) functionally derivatising the carboxylic acid or related group in which the third irregularly branch amidoamine aiming unit terminates.

40. A composition comprising a hyperbranched amidoamine  
20 polymer together with an agent selected from the group consisting of a therapeutically or prophylactically active agent, an *in vivo* occurring or *in vitro* generated nucleotide, a diagnostic agent, a pesticide, a toxin, a protein, an antigen, a peptide, a nucleic acid, an amino  
25 acid and a bioactive agent.

41. A composition according to claim 40, selected from the group consisting of compositions wherein the nucleotide is selected from the group consisting of a  
30 polynucleotide, an oligonucleotide, a virus or a fragment thereof, an expression vector, gene or fragment thereof, DNA, RNA, compositions wherein the diagnostic agent is a diagnostic contrast agent selected from the group

consisting of a radionuclidic, paramagnetic, superparamagnetic, ferromagnetic, ferrimagnetic, antiferromagnetic, diamagnetic, fluorescent, phosphorescent, luminescent, chemiluminescent, X-ray  
5 absorbent, UV absorbent, IR absorbent and ultrasound absorbent species, and compositions wherein the protein is selected from the group consisting of an immunoglobulin, an antibody, and fragments thereof.

10 42. A composition according to claim 40, selected from the group consisting of compositions wherein the hyperbranched amidoamine polymer is coupled with the agent, compositions wherein the hyperbranched amidoamine polymer encapsulates the agent, compositions wherein the  
15 hyperbranched amidoamine polymer is complexed with the agent and compositions wherein the hyperbranched amidoamine polymer is bound to the agent.

43. A composition according to claim 42, wherein the  
20 hyperbranched amidoamine polymer is bound to a compound selected from the group consisting of a nucleotide, a polynucleotide, a virus or fragment thereof, an expression vector, a gene or fragment thereof, DNA, and RNA.

25 44. An *in vivo* transfection agent comprising an aqueous solution of a hyperbranched amidoamine polymer.

45. A hyperbranched amidoamine polymer or a composition  
30 thereof for use in therapy or prophylaxy.

46. A hyperbranched amidoamine polymer or composition thereof according to claim 45, wherein the hyperbranched amidoamine polymer is a polymer according to claim 1.

5 47. A hyperbranched amidoamine polymer or composition according to claim 45, wherein the use of the hyperbranched amidoamine polymer is selected from the group consisting of use as a delivery agent for a therapeutically or prophylactically active agent, use in  
10 gene therapy or prophylaxy, use as a nucleotide carrier, use as a transfection agent and use as a vector.

48. Use of a hyperbranched amidoamine polymer as a carrier, substrate or support.

15 49. Use according to claim 48, wherein the use of the hyperbranched amidoamine polymer is selected from the group consisting of use as a nucleotide carrier, use as a transfection agent, use as a vector, use as a support,  
20 use as a substrate, use in combinatorial chemistry, use in catalysis, use in surface coating, use in implant coating and use in a photoactive system.

50. Use of a hyperbranched amidoamine polymer in the  
25 preparation of a medicament for treating or preventing a genetically related condition or disorder.

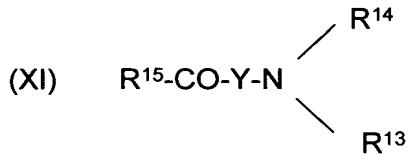
51. Use according to claim 49, wherein the hyperbranched polyamidoamine is as claimed in claim 1.

30 52. A hyperbranched polymer comprising amidoamine groups, wherein greater than 80% of the terminal groups are functional amine groups.

53. A polymer according to claim 52, wherein the functionalised amine groups are protonated.

5 54. A composition comprising a hyperbranched polymer having less than 20% of methyl ester terminal groups, bound to a compound selected from the group consisting of a nucleotide, a polynucleotide, a virus or fragment thereof, an expression vector, a gene or fragment  
10 thereof, DNA, and RNA.

55. A compound of formula:



15 wherein:

Y is as hereinbefore defined;

$R^{15}$  as hereinbefore defined for group T;

Each of  $R^{13}$  and  $R^{14}$ , which may be the same or different, is a group  $-Y'-CO-NH-X-NH_2-Y'-CO-NH-X-NR^{16}-(Y''-CO-NH-X'-NR^{17}R^{18})$ , wherein  $R^{16}$  is selected from the group consisting of hydrogen and  $-Y''-CO-NH-X'-NR^{17}-R^{18}$ ; each of  $R^{17}$  and  $R^{18}$ , which may be the same or different is selected from the group consisting of hydrogen and  $-Y'''-CO-NH-X''-NR^{19}R^{20}$ , wherein each of  $R^{19}$  and  $R^{20}$ , which may be the same or different, is selected from the group consisting of hydrogen and  $-Y''''-CO-NH-X''''-NH^2$ ; and

$Y'$ ,  $X$ ,  $X'$ ,  $X''$ ,  $X'''$ ,  $Y'''$ ,  $Y''''$  and  $Y''$  are as hereinbefore defined.

56. A compound according to claim 55, selected from the group consisting of compounds wherein  $R^{13}$  and  $R^{14}$  are both the group  $-Y'-CO-NH-X-NH_2$ , compounds wherein  $R^{13}$  and  $R^{14}$  are both the group  $-Y'-CO-NH-X-N-(Y''-CO-NH-X'-NH_2)_2$ ,

5 compounds wherein  $R^{13}$  and  $R^{14}$  are both the group  $-Y'-CO-NH-X-N-(Y''-CO-NH-X'-N(Y'''-CO-NH-X''-NH_2)_2)_2$ , and compounds wherein  $R^{13}$  and  $R^{14}$  are both the group  $-Y'-CO-NH-X-N-(Y''-CO-NH-X'-N(Y'''-CO-NH-X''-N(Y''''-CO-NH-X''''-NH_2)_2)_2$ .